

012103

02570 U.S. PTO

USE OF INHIBITORS OF MAMMALIAN ASPARAGINYL ENDOPEPTIDASE FOR...

Colin Watts

Appl. No.: 09/646,950 Atty Docket: ERP01.004APC

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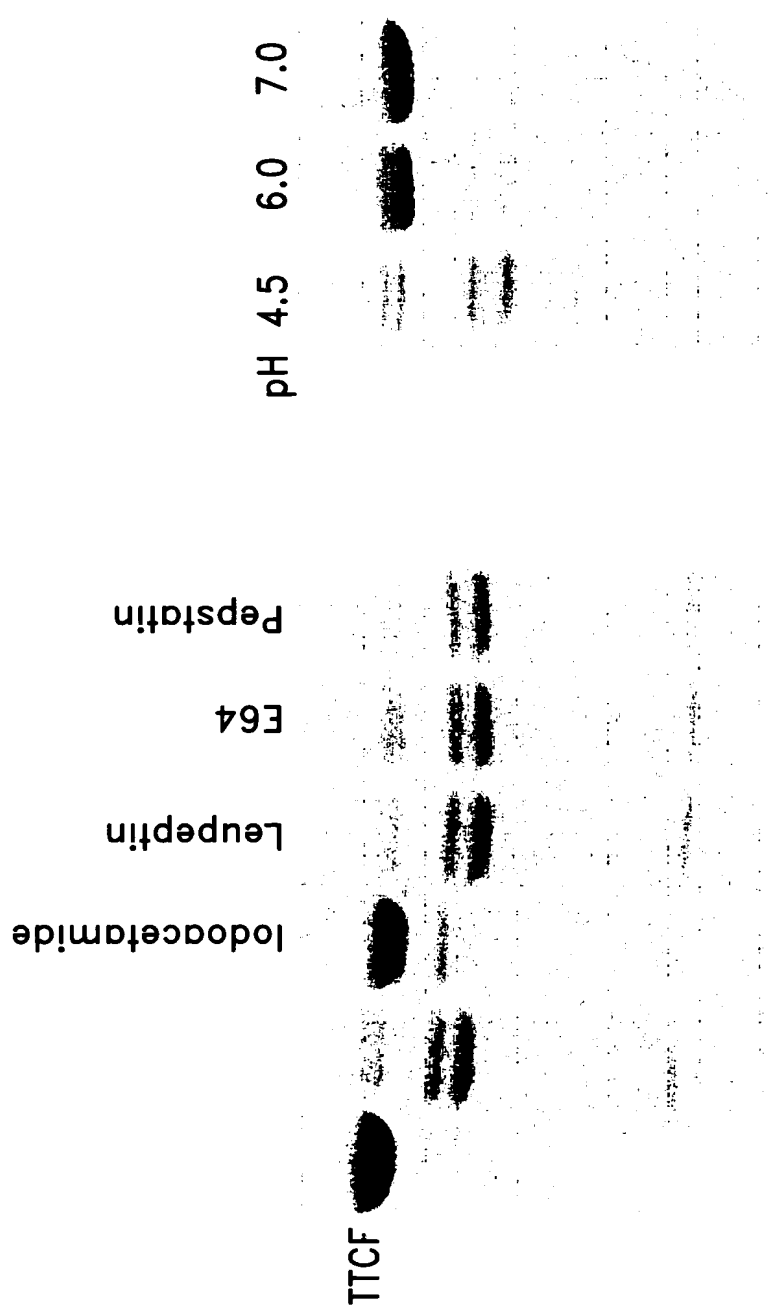


FIG. 1A

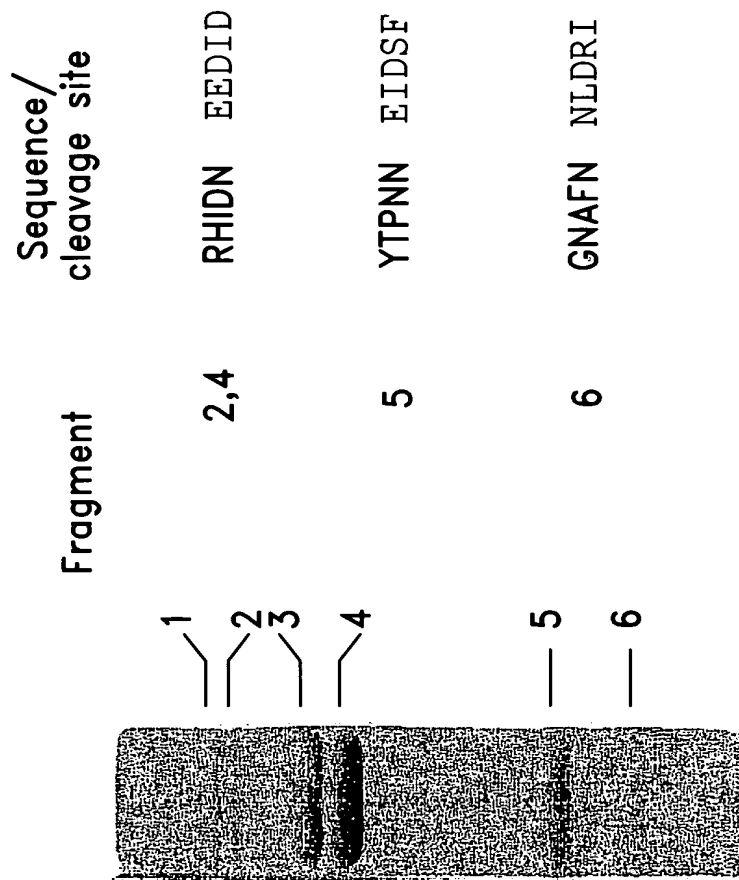


FIG. 1B

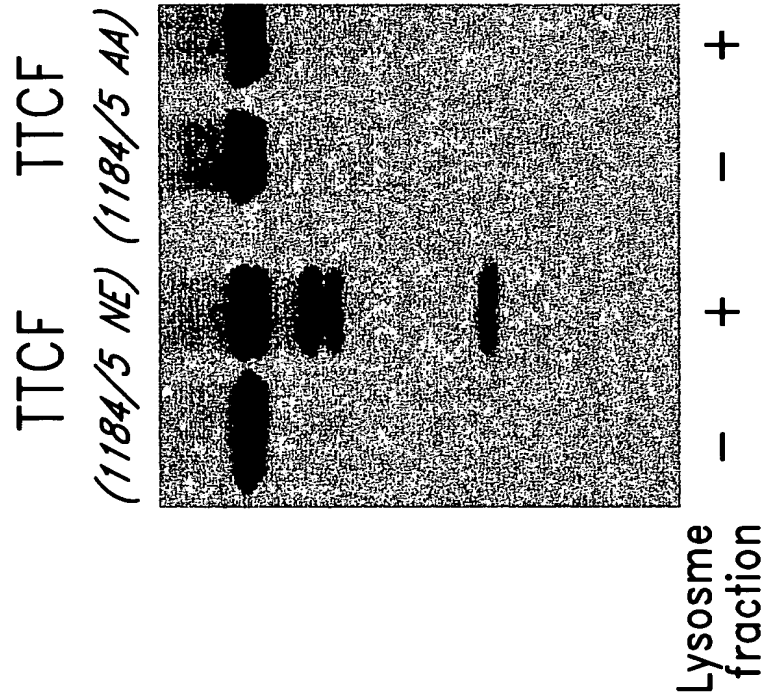


FIG. 1C

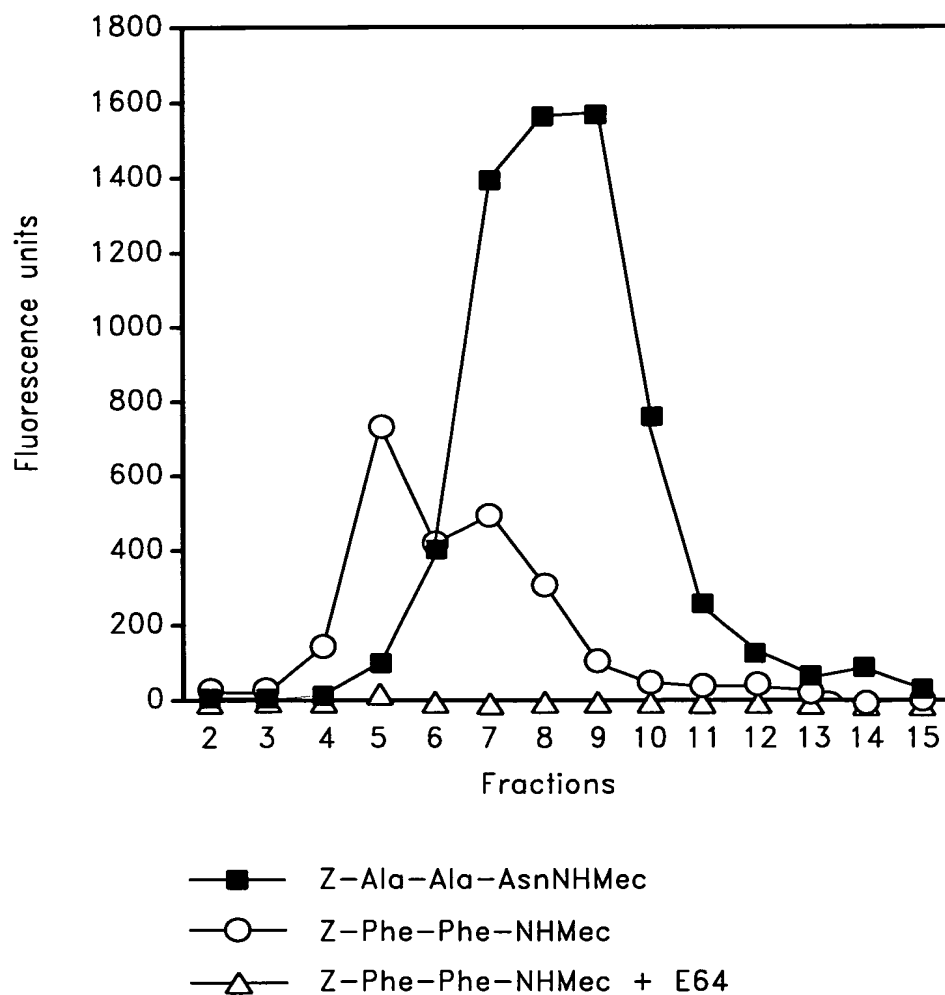


FIG. 2A

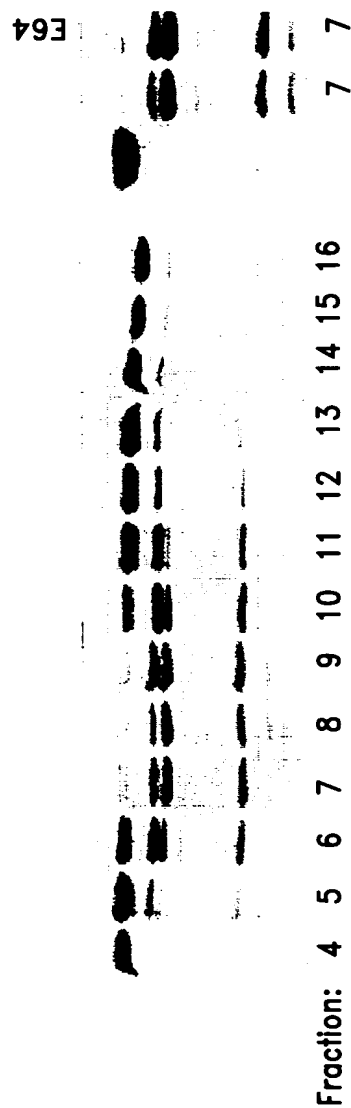


FIG. 2B

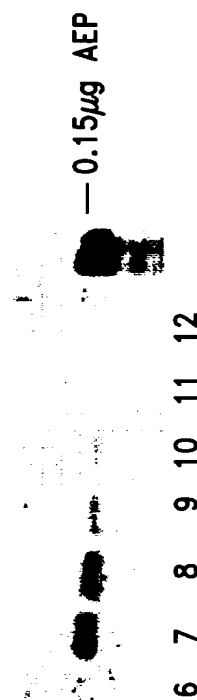


FIG. 2C

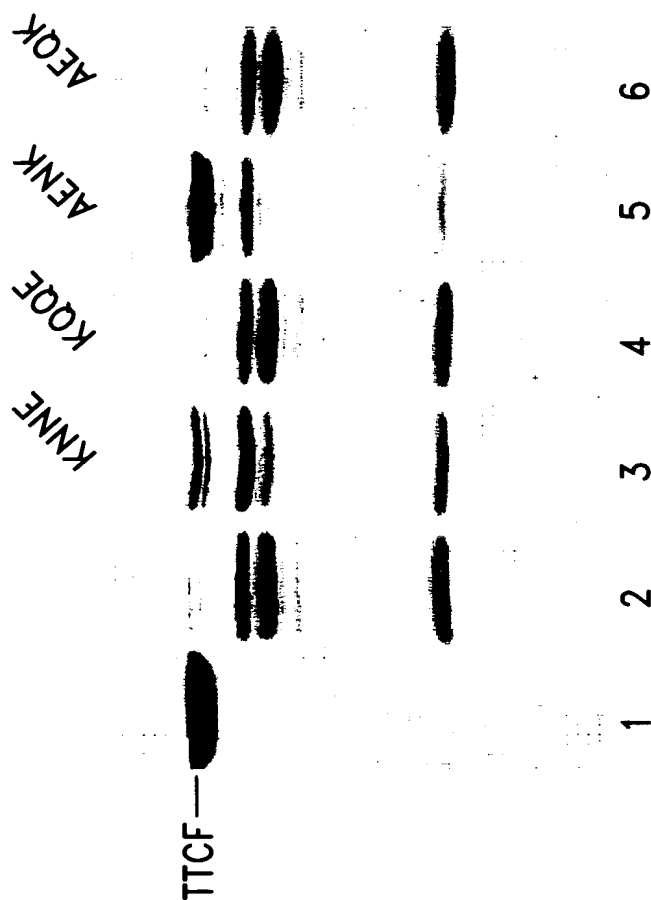


FIG. 3A



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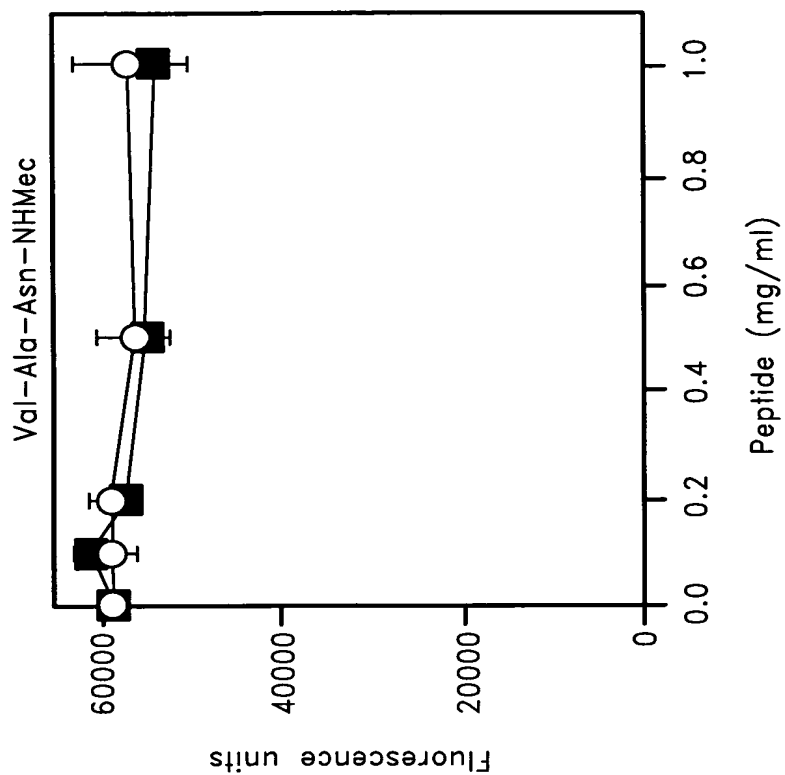
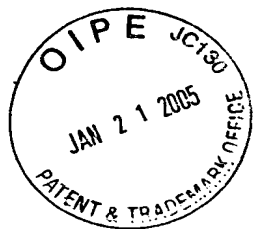


FIG. 3B<sub>2</sub>

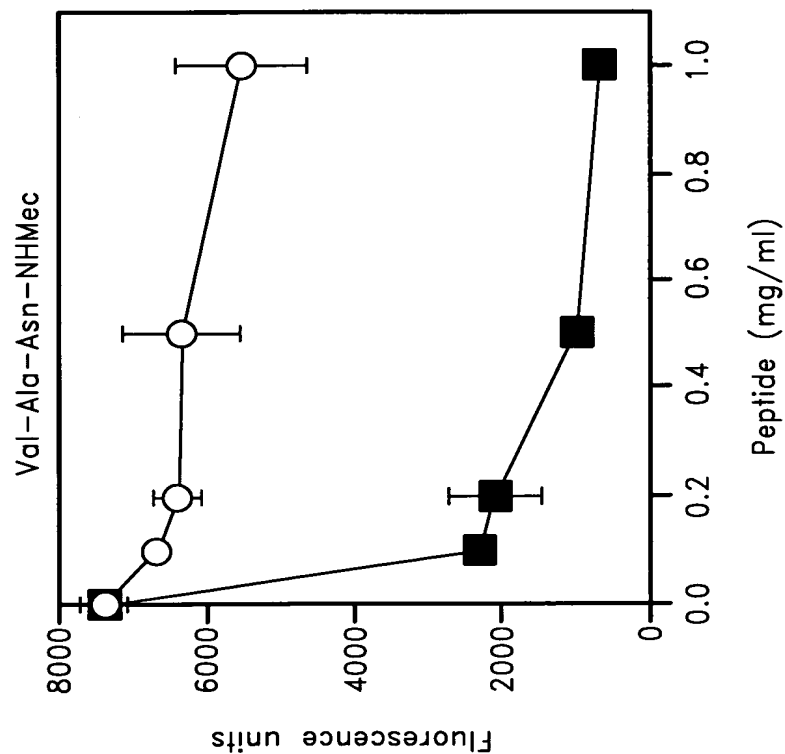


FIG. 3B<sub>1</sub>

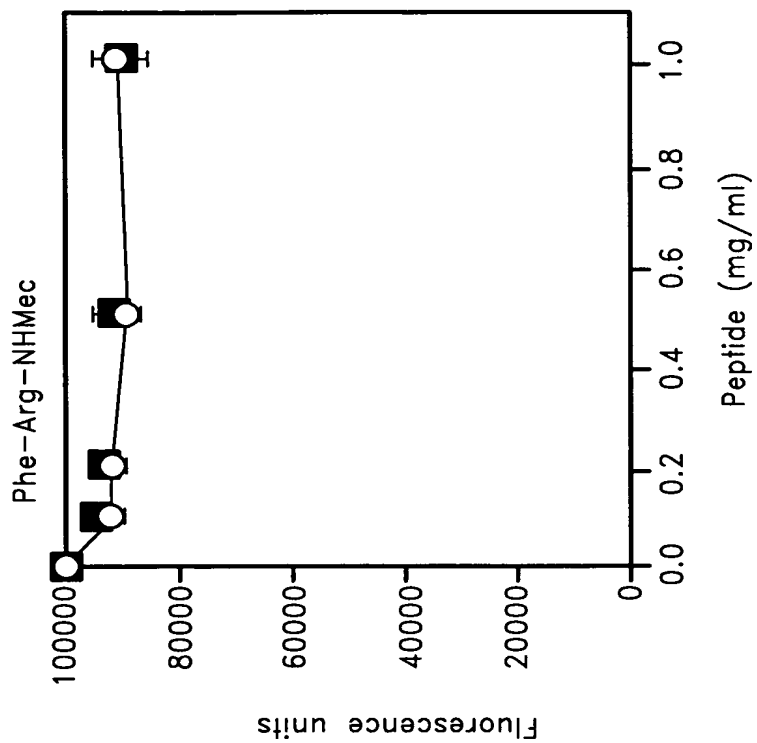
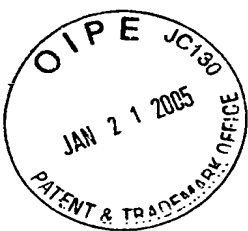


FIG. 3B<sub>4</sub>

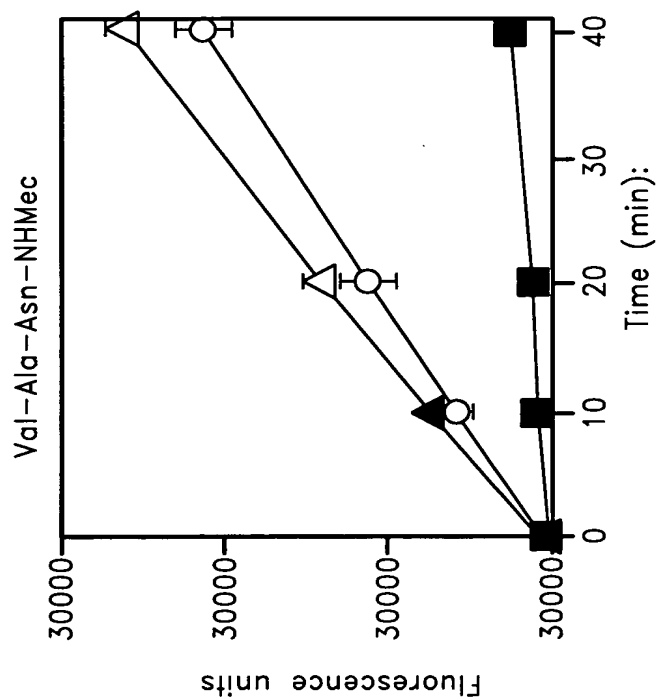


FIG. 3B<sub>3</sub>



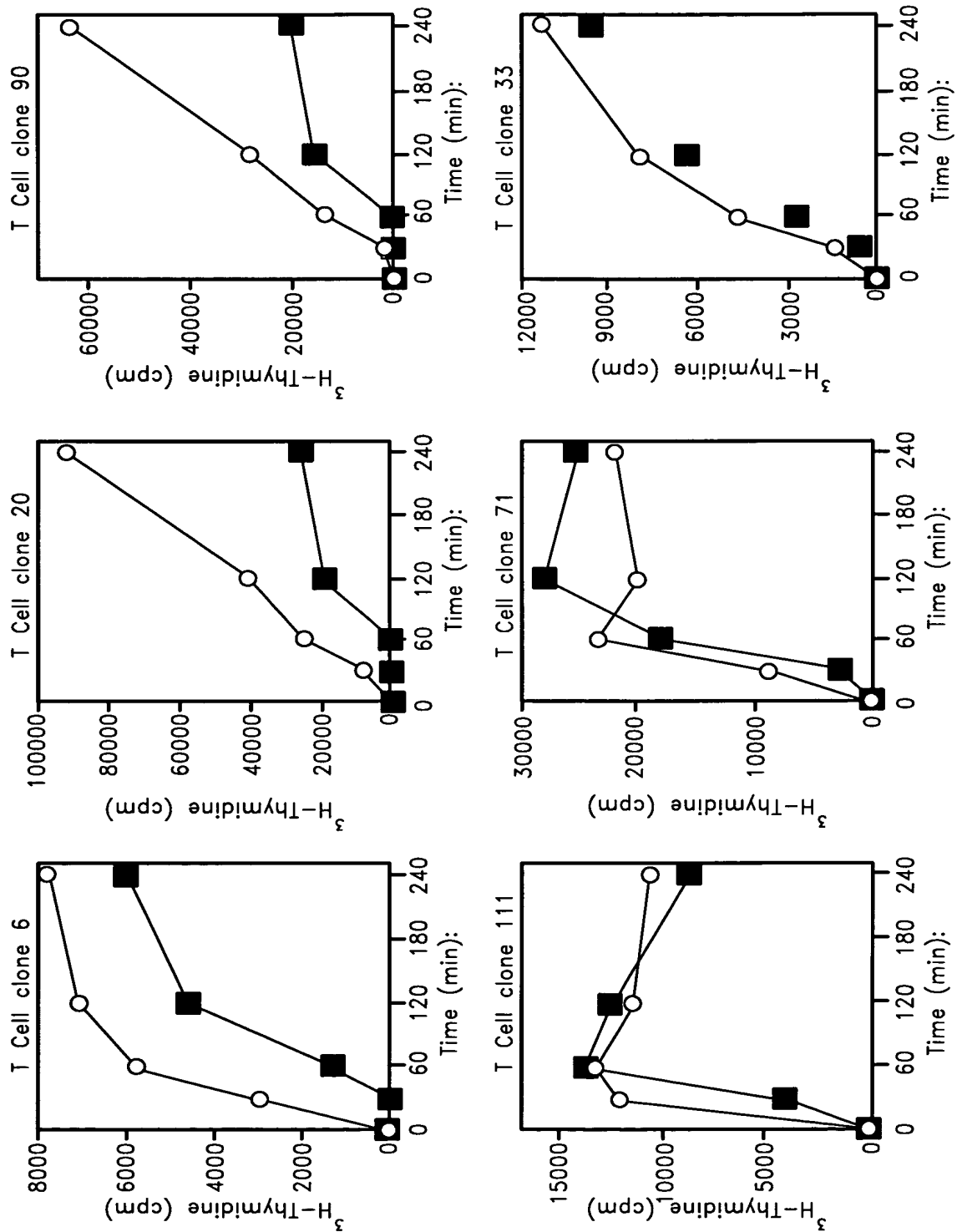
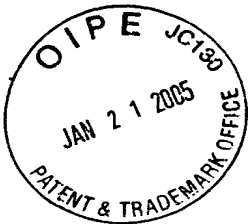
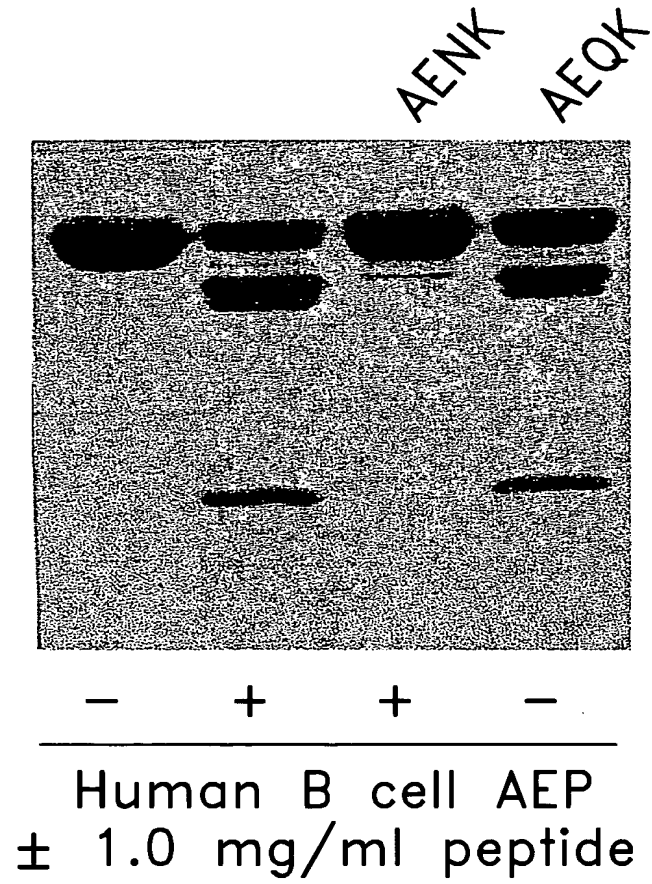


FIG. 3C

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*FIG. 3D*

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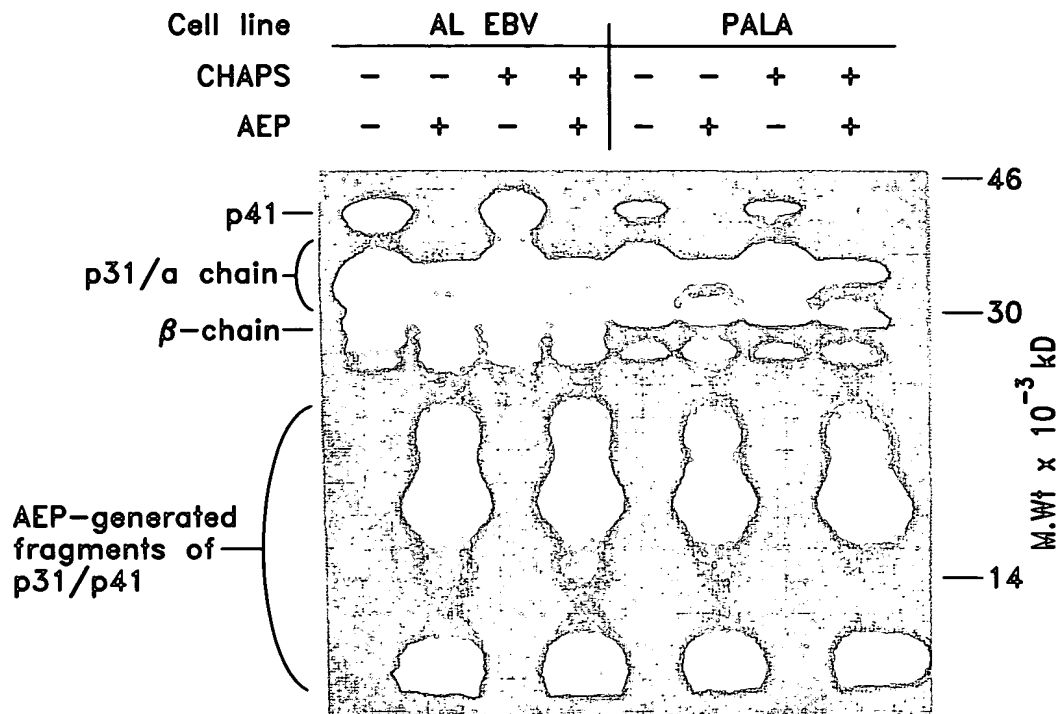


FIG. 4

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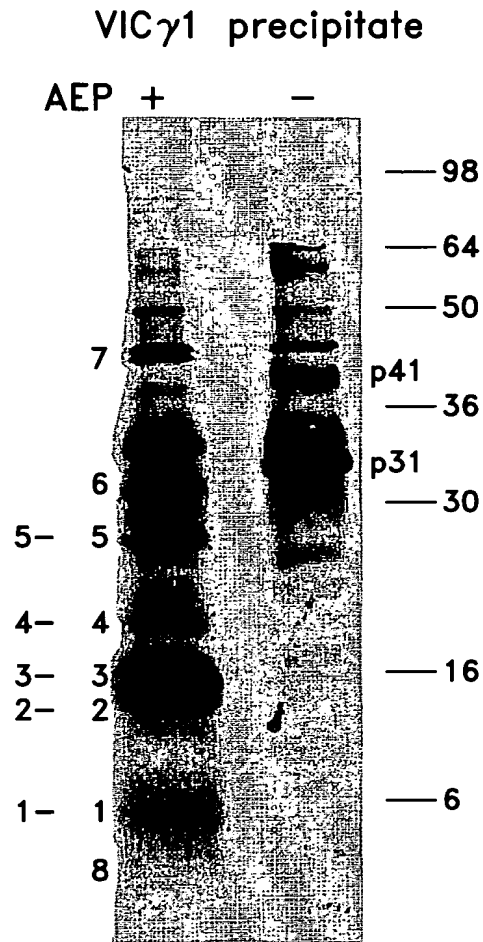
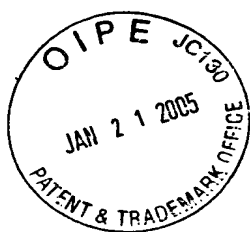


FIG. 5A



N-terminal sequence of bands below

Band 1: N NEQLPM (Peak cycle 5/6)

Band 2: N TMETI (Peak cycle 2)

Band 3: N LRMK (Peak cycle 3)

Band 4: N LRMK  
N NEQLPM (Peaks at cycles 3 & 6)

Band 5: N LRMK

Example raw data from band 5

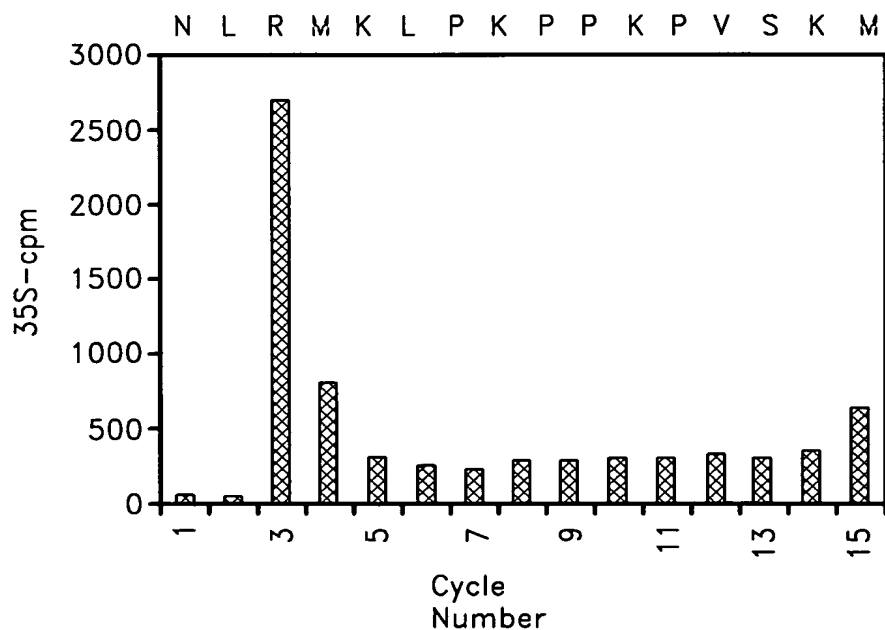
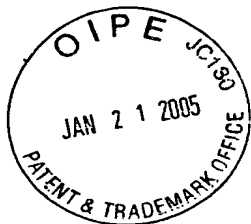


FIG. 5B



↓  
MDDQRLDISNNEQLPMLGRRPGAPESKCSRGALYTGFSILVTLLLAGQATTAYF  
↓  
QQQGRLDKLTVTSONLQLENLRMKLPKPPKPVSKMRMATPLLMQALPMGALPQG  
↓  
QNATKYGNMTEDHVMHLLQNADPLKVYPPPLKGSFPENLTHLKNMTMETIDWKVFE  
MHHWLLFEMSRHSLEQKPTDAPPKESLELEDPSGLGVTKQDLGPVPM

FIG. 5C



Identified AEP cleavage sites

Tetanus toxin C fragment

RHIDN EEDID  
YTPNN EIDSF  
GNAFN NLDRI

Ribonuclease

NGQTN CYQSY  
VACKN GQTNC

Ovalbumin

GTSVN VHSSL

Hen Egg Lysozyme  
(preferred sites listed  
first)

GNGMN AWVAW  
HGLDN YRGYS  
ILQIN SRWWC  
VSDGN GMNAW  
RWWCN DGRTP  
VAWRN RCKGT

Transferrin peptide  
(622-642)

LFGSN VTDCS  
DCSGN FCLFR

*FIG. 6*



FIG. 7A

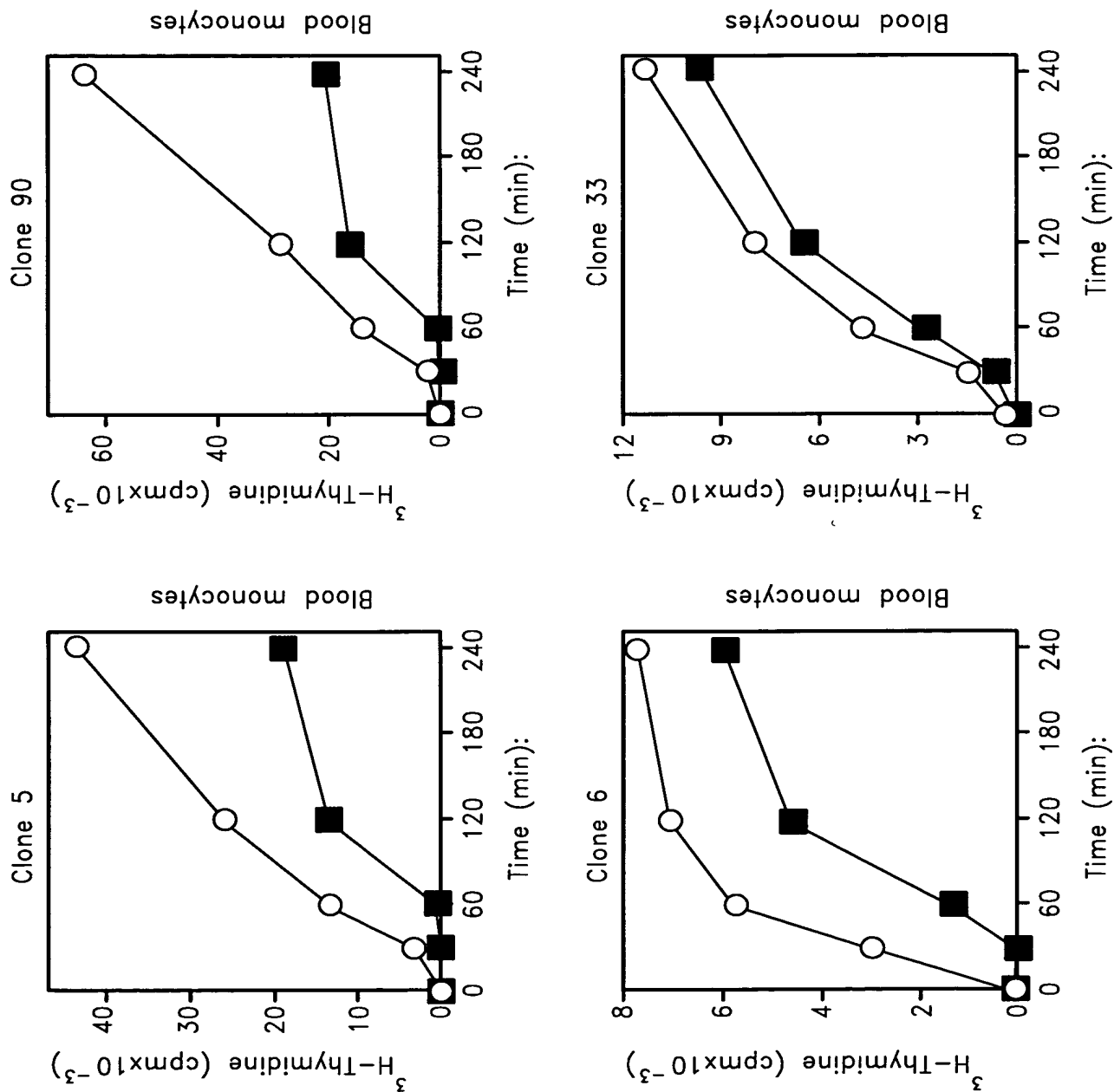
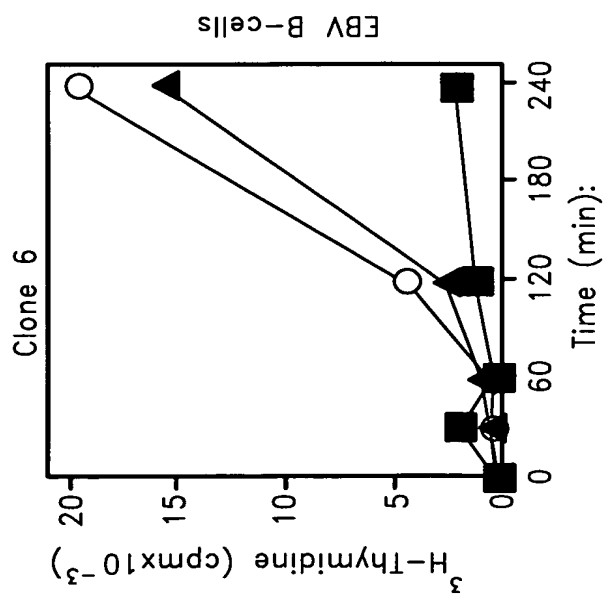
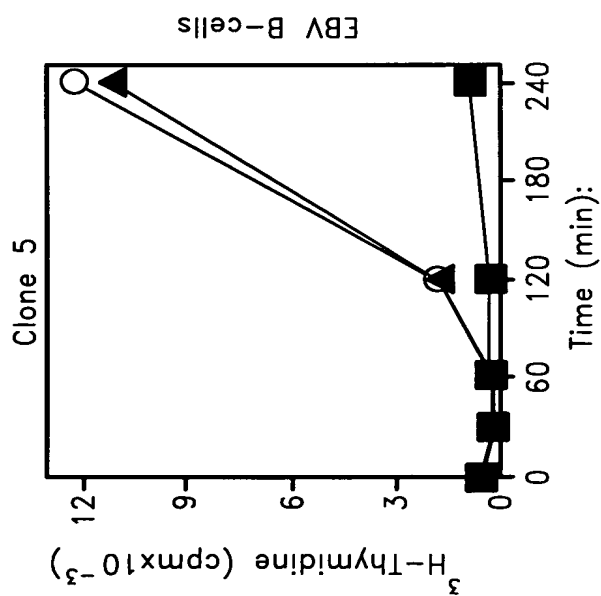
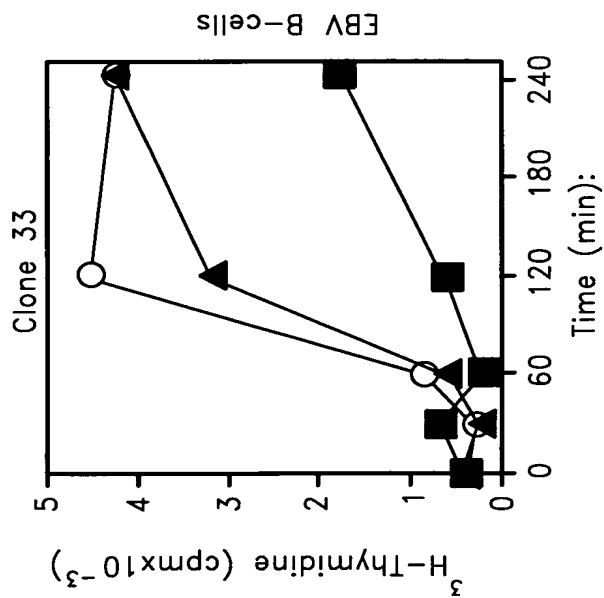
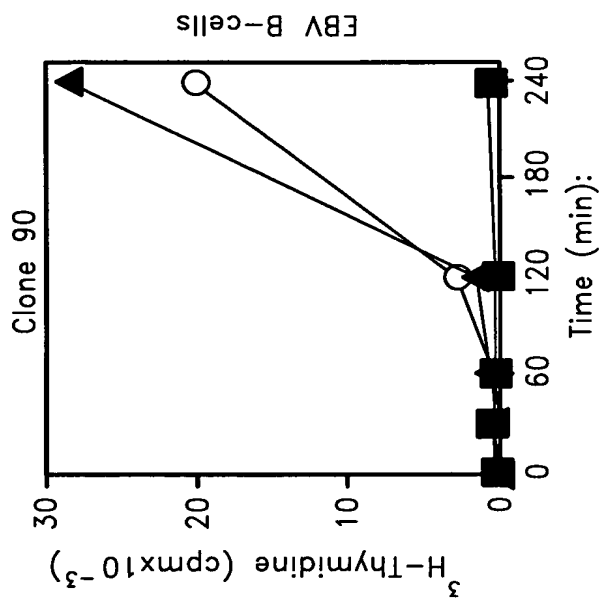






FIG. 7B



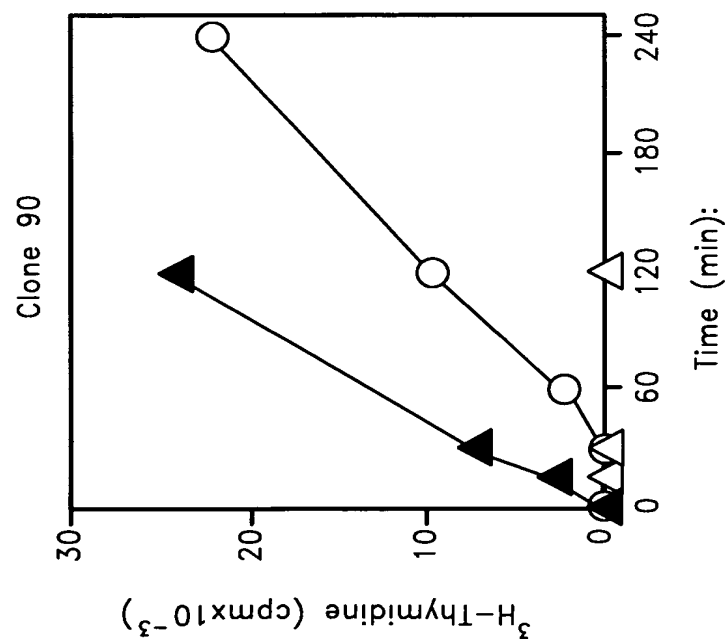
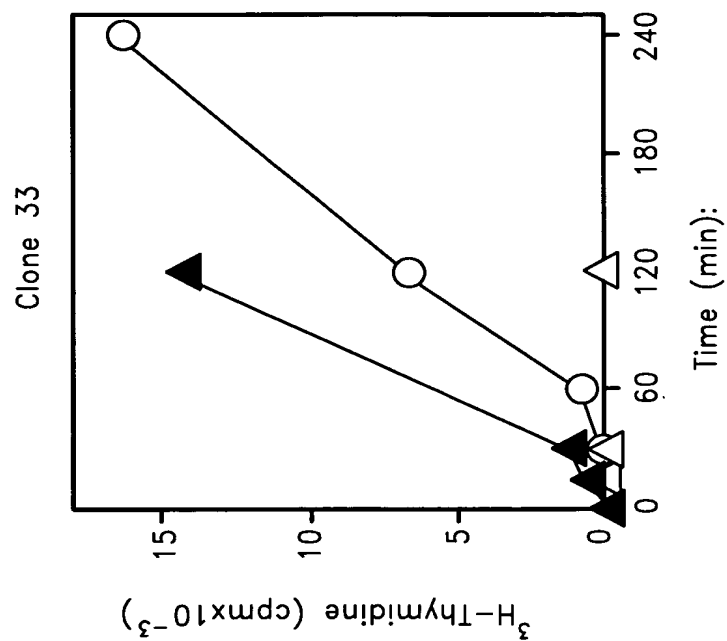


FIG. 7C

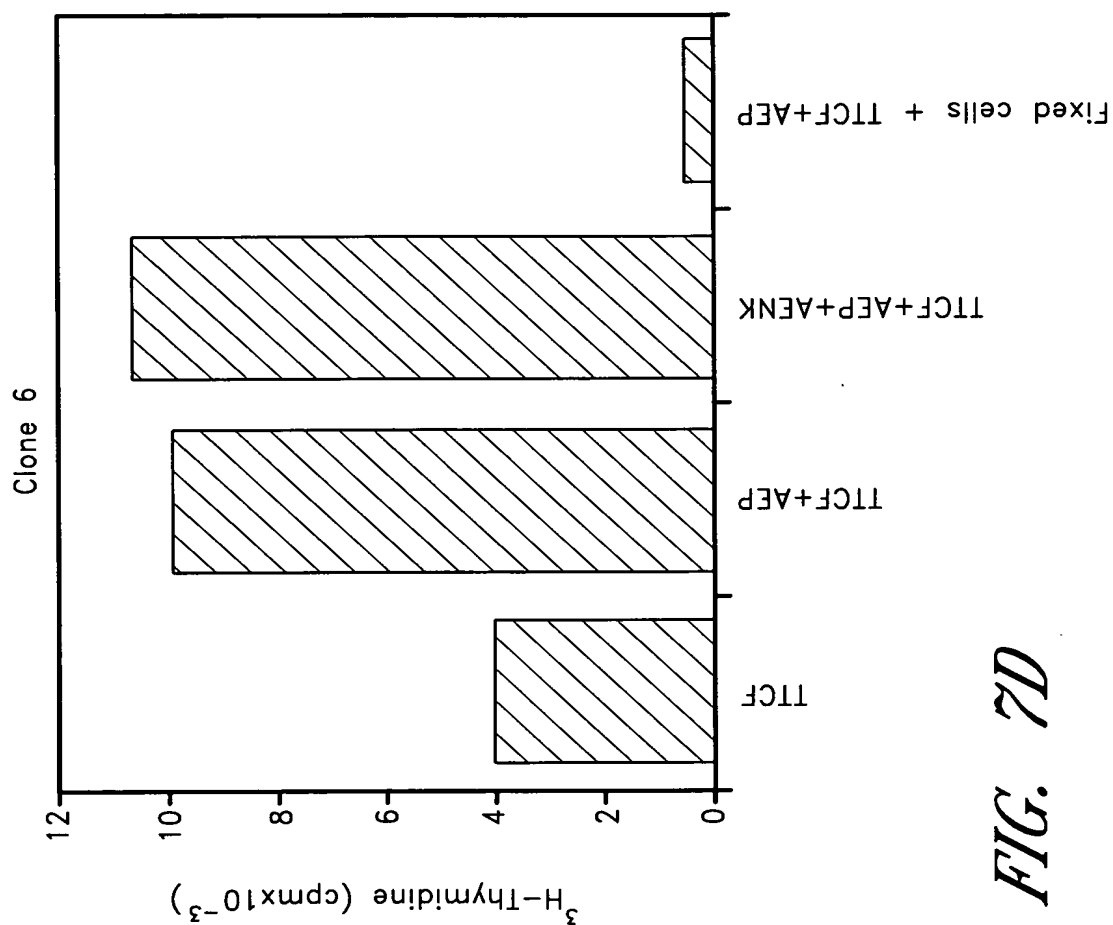


FIG. 7D